REMARKS

The Amendments

Claims 1 and 37 are amended to remove the "hydrate" recitation and to correct the typographical error noted in the Office action.

It is submitted that the above amendments would put the application in condition for allowance or materially reduce or simplify the issues for appeal. The amendments do not raise new issues or present new matter and do not present additional claims. The amendments have been made to render moot the existing 35 U.S.C. §112 and claim objection issues raised in the Final action, thus simplifying the issues. Thus, they were not earlier presented. Accordingly, it is submitted that the requested amendments should be entered.

Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Withdrawn Claims

The claims withdrawn from consideration are withdrawn pursuant to an election of species requirement, not a restriction requirement (see the Office actions of August 18, 2008, and November 13, 2008). Since the elected subject matter is believed to be in condition for allowance (for the reasons provided here), the examination should be extended to include the non-elected subject matter. Further, applicants urge that the allowability of the non-elected subject matter should be clear from the allowability of the elected subject matter.

The Claim Objection

The objection to claim 1 is rendered moot by the above amendment (an analogous amendment was made in claim 37).

The Rejections under 35 U.S.C. §112

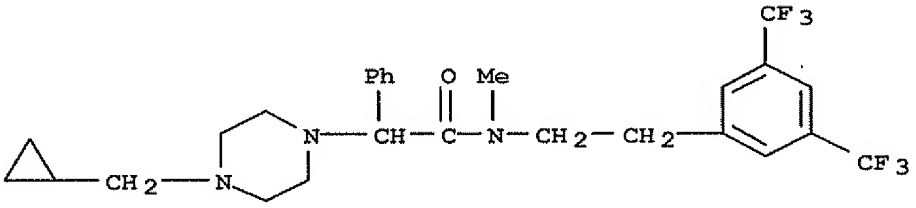
The rejections under 35 U.S.C. §112, for lack of adequate written description and

enablement, are rendered moot by the cancellation of the "hydrates" term in the claims. Although applicants remain of the opinion that the hydrates are adequately described and enabled, the amendment is made to advance prosecution without prejudice to a continuing application directed to this subject matter.

The Rejections under 35 U.S.C. §103

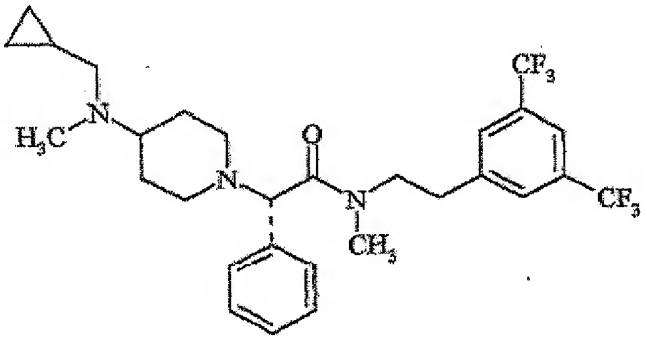
The rejection of claims 1-3, 5, 7-10, 20-26, 28-31, 35 and 37 under 35 U.S.C. §103, as being obvious over Meissner (U.S. Pub. No. 2002/0115680) in view of Dollinger (WO 02/32865, U.S. Patent No. 6,747,044 equivalent) and Podolsky (US Pub. No. 2003/185838), and the rejection of claim 27 under 35 U.S.C. §103 over these references further in view of Freund (US Pub. No. 2001/0008632), are respectfully traversed.

The rejections are based on an erroneous interpretation of the Dollinger reference. Dollinger does not teach any of the NK1 receptor antagonists recited in applicants' independent claims 1 or 37. Thus, even if the references are properly combined, such combination would not arrive at or suggest the claimed invention because none of the cited references give one of ordinary skill in the art a reason to include an NK1 receptor antagonist as recited in applicants' claims in a composition. The first NK1 receptor antagonist recited in current claims 1 and 37 is named "(S)-N-[2-[3,5-bis(trifluoromethyl)phenyl]ethyl]-4-(cyclopropylmethyl)-N-methyl-α-phenyl-1-piperazineacetamide." The structure of this compound is as follows:



The compound of Example 3 of Dollinger (pages 16-17 of the WO publication, cols. 11-12, of the US patent) is recited as "N-[2-(3,5-bis-trifluormethyl-phenyl)-ethyl]-2-[4-(cyclopropylmethyl-methyl-amino)-piperidin-1-yl]-N-methyl-2-phenyl-acetamid." The names of

the two structures clearly show their difference. Although the right side of each structure is the same and the left side has some similarities, it is clearly different. The NK1 antagonist recited for use in the claimed invention contains a piperazine group substituted on the 4-nitrogen with cyclopropylmethyl whereas the Dollinger compound has a piperidine ring substituted at the 4-carbon with cyclopropylmethyl-methyl-(N-methyl)amino. The structure of the Dollinger compound (which is the last compound shown on page 8 of the Dollinger WO publication) is:



The NK1 antagonists disclosed by Dollinger do not teach or suggest the NK1 antagonists recited in applicants' claimed compositions. Meissner and Podolsky also fail to provide any teaching or suggestion of the NK1 antagonists recited in applicants' claimed compositions. Since none of the cited references provide one of ordinary skill in the art to include any of the specific NK1 antagonists recited in applicants' claimed compositions in a composition, the claimed compositions cannot be rendered obvious by the combined reference teachings. See, e.g., KSR International Co. v. Teleflex Inc., 550 U.S. _, 82 USPQ2d 1385, at 1396 (2007), stating: "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness."

Applicants believe the rejections are overcome when considered in view of the correct interpretation of the Dollinger reference. But for completeness of the record, applicants address the Response to Arguments section of the Final Office action in the immediately following paragraph and, in the following paragraphs, reiterate their previous arguments for nonobviousness.

It is alleged in the Office action that applicants' arguments are deficient for attacking the references individually rather than their combination. While including some discussion of the references individually, applicants clearly did address the combined teachings of the references. The Office action itself makes clear that applicants provided arguments based on the combined teachings of the references. To address the combined teachings of the references, it is necessary to establish what each discloses individually. There is nothing improper in this manner of argument. It is further alleged in the Office action that Dollinger teaches a specific NK1 receptor antagonist as recited in applicants' claims. As pointed out above, this allegation is not supported by the reference teaching. The Dollinger compounds are not the same. The Office action points to Example 8 of Podolsky as teaching treating lesions "**caused by smoke inhalation**" with NK antagonists and equates this to a teaching of treating COPD. However, in Example 8 of Podolsky, only the trefoil peptide (ITF compound) is used, not any NK antagonist. Further, applicants do not believe the PTO has met its burden of proving that treatment of a symptom also connected with COPD equates to treating the underlying condition of COPD, for the reasons stated below. The disclosure in paragraphs 0059-0060 of the instant specification (page 10) does not equate treating only a symptom with treating the underlying disease. Applicants' disclosure here teaches that treating COPD can include additionally treating certain complications (symptoms) thereof, not merely treating the symptom. It is not taught that treating the symptom alone is equated to treating the underlying disease. The claimed method requires treating the underlying condition, not merely some symptom thereof. Thus, the facts are directly analogous to the Rapoport case.

Meissner discloses compounds of its formula I as anticholinergics, particularly for treating asthma or COPD (chronic obstructive pulmonary disease). Meissner does not provide any suggestion of a composition of such compounds together with an NK_1 receptor antagonist.

Dollinger discloses compounds of the formula (I) (col. 1) as being neurokinin antagonists. Dollinger teaches that the compounds are useful for, among other things, treating COPD. The neurokinin antagonists disclosed by Dollinger are not included in the neurokinin receptor antagonist component used in the claimed compositions (as discussed above). Thus, to the extent the rejection is based on a suggestion to combine the anticholinergic of Meissner with a

neurokinin antagonist disclosed by Dollinger, such a combination would not result in or suggest the currently claimed invention.

Podolsky teaches that specific trefoil peptide compounds may be used to treat lesions of the respiratory epithelium. Podolsky discloses that the lesions being treated can result from a wide variety of causes (see, e.g., page 1, paras. 0004 and 0010). Such lesions are not necessarily connected with COPD but are a symptom which can arise as a consequence of many of a variety of circumstances or diseases, for instance, from such varied sources as surgical intervention or intubation or by inhaling smoke, etc. (see, e.g., page 3, para. 0032, of Podolsky). Podolsky discloses that its specific trefoil peptides may optionally be used in combination with second therapeutic agents. Podolsky discloses a large variety of general second therapeutic agents which could possibly be used, i.e., anti-inflammatory agents, non-steroidal anti-inflammatory agents, antimicrobial agents, antihistamines, cholinergic receptor antagonists, neurokinin receptor antagonists, leukotriene receptor antagonists, decongestants, phosphodiesterase inhibitors and beta-adrenergic antagonists (see, e.g., page 1, para. 0012).

One of ordinary skill in the art is not taught by Podolsky that its trefoil peptides or its second therapeutic agents are effective to treat COPD but merely for treating a symptom which might arise from COPD or from any of a number of other varied sources. Lesions of the respiratory epithelium are only in certain situations connected with COPD, i.e., lesions of the epithelium are not a general symptom in COPD. Further, lesions of the respiratory epithelium can also be caused by many different diseases and circumstances other than COPD. Contrary to the allegation in the Office action (page 11), Podolsky does not "expressly teach the administration of neurokinin receptor antagonists in combination with trefoil peptides in the treatment of COPD." First, there is no specific disclosure of a combination of a trefoil peptide with a neurokinin receptor antagonist in Podolsky. Second, as discussed above, Podolsky only teaches treating lesions of the respiratory epithelium which can be a symptom of COPD but does not disclose or suggest treating COPD itself.

Contrary to the allegation in the Office action (page 15), Podolsky does not expressly teach that NK1 receptor antagonists are useful for treating COPD. Podolsky suggests treatment of a symptom of COPD – not the underlying disease. It should be evident that treatment of a

symptom does not necessitate or suggest treating the disease. In fact, the Federal Circuit has addressed this very issue and found that a prior art teaching to use an agent to treat one possible symptom of a disease or condition does not amount to a teaching to use the agent to treat the disease or condition itself. See, e.g., Rapoport v. Dement, 254 F.3d 1053, 59 USPQ2d 1215 (Fed. Cir. 2001), finding that treating a symptom of sleep apnea was not the same invention as treating sleep apnea. The Court rejected Rapoport's argument that a count was unpatentable on the ground that the prior art disclosed administering the compound – not for treatment of sleep apnea itself – but for treatment of anxiety and breathing difficulty, a symptom of apnea, stating: "There is no disclosure in the [prior art reference that the compound] is administered to patients suffering from sleep apnea with the intent to cure the underlying condition." The facts are directly analogous here and the same reasoning of the Court should apply. A teaching to treat the symptom of lesions of the epithelium is not a teaching to treat the underlying condition of COPD.

Additionally, considering the combined teachings of the prior art as a whole, one of ordinary skill in the art would not have been motivated by the reference teachings or have any other reason to combine one of the second therapeutic agents of Podolsky into the Meissner compositions or methods. Meissner is directed to methods and medicaments for treating COPD, whereas Podolsky is directed to methods and medicaments for treating lesions of the respiratory epithelium. As discussed above, these are different methods. Further, even if treating lesions of the respiratory epithelium were considered to also treat COPD – which is not supported on the record – Podolsky still only suggests that its specific trefoil peptides are useful for treating lesions of the respiratory epithelium. Podolsky does not teach what effect the secondary agents may have or that they would be useful for treating lesions of the respiratory epithelium. Thus, one of ordinary skill in the art could not have a reasonable expectation that the second therapeutic agents, particularly a specific selected one of them, would be effective without being combined with the trefoil peptides which are the main focus of Podolsky.

Even if, contrary to all of the above reasons, one of ordinary skill in the art did have a reason to combine a second therapeutic agent of Podolsky into the Meissner compositions/methods, the claimed invention would still not be suggested. Podolsky lists "neurokinin receptor antagonists" as only one broad category among a wide variety of possible

second therapeutic agents. Given the broad teaching, one of ordinary skill in the art would not have been fairly directed to select this specific category of agent to combine with Meissner, particularly in view of the other distinctions discussed above. Further, Podolsky's teaching of "neurokinin receptor antagonists" does not point one of ordinary skill in the art to the specifically claimed invention, even if this category was selected. Podolsky does not teach, specifically, NK_1 antagonists (i.e., neurokinin receptor type 1 antagonists). There are at least three known neurokinin receptors types and nothing in the art points one of ordinary skill in the art to specifically select the NK_1 antagonists.

Further, each of Meissner, Dollinger and Podolsky are silent as to the combined effect of an anticholinergic and NK_1 receptor antagonist. There is no suggestion that these compounds would be compatible or that their combination would be reasonably expected to succeed for treating a respiratory disease, particularly COPD, or for any other reason.

Finally, none of the cited references provides any teaching at all regarding the specific NK_1 antagonists now recited in the independent claims. As discussed above, Dollinger is the only reference which relates to specific NK_1 antagonists. But the compounds of Dollinger are distinct from those recited in the instant claims. None of the references suggest that the compounds recited for the second components in the claimed compositions are NK1 antagonists or that these specific compounds should be combined with the specific anticholinergic of applicants' formula 1 for the purpose of treating COPD or for any other purpose.

Regarding the rejection of claim 27 further in view of Freund, the additional reference was cited for its teachings of adding an antioxidant. Freund fails to make up for the above-noted deficiencies of the primary references. Thus, this rejection is overcome for the same reasons.

For all of the above reasons, it is urged that the combined teachings of the prior art fail to render the claimed invention obvious to one of ordinary skill in the art and the rejections under 35 U.S.C. §103 should be withdrawn.

It is submitted that the application is in condition for allowance. But the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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